

Critical Reviews in Toxicology



ISSN: 1040-8444 (Print) 1547-6898 (Online) Journal homepage: http://www.tandfonline.com/loi/itxc20

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To cite this article: Roger O. McClellan (2016) Evaluating the potential carcinogenic hazard of glyphosate, Critical Reviews in Toxicology, 46:sup1, 1-2, DOI: 10.1080/10408444.2016.1234117

To link to this article: http://dx.doi.org/10.1080/10408444.2016.1234117

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	Published online: 28 Sep 2016.
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FOREWORD 3 OPEN ACCESS

Evaluating the potential carcinogenic hazard of glyphosate

Critical Reviews in Toxicology (CRT) has been a leader for more than four decades in publishing scientific reviews evaluating the health hazards of exposure to chemicals that are widely used around the globe. These reviews have been internationally recognized for their comprehensive coverage of contemporary topics ranging from novel testing and assessment strategies to the characterization of the potential hazards associated with chemicals. The reviews evaluating potential chemical hazards and risk typically cover and integrate evidence from multiple avenues of investigation, including molecular and cellular research, animal investigations and epidemiological studies. From its first issue in 1971 to the present, CRT has a well-earned reputation for scientific rigor and thoroughness of its external peer review.

This Special Issue of CRT contains five papers each addressing aspects of the evaluation of the potential carcinogenic hazard of glyphosate, a chemical discovered by a scientist at Monsanto Company in 1970. Glyphosate was rapidly commercialized and initially marketed in 1974 as Roundup. Since going off patent in 2000, glyphosate has been produced and marketed by a growing number of companies. It is one of the most widely used agricultural chemicals in the world and has been of great benefit in weed control and enhanced productivity of a number of crops.

Monsanto conducted the first safety evaluations on glyphosate prior to marketing of products containing the chemical. These in-house evaluations were followed by review and approval for marketing by the U.S. Environmental Protection Agency and then other government agencies around the world. Scientific information available on the potential health hazards of glyphosate continues to increase and is now voluminous.

The International Agency for Research on Cancer (IARC) announced in 2014 that it was going to review glyphosate along with four pesticides for their potential carcinogenic hazard. Four review papers, commissioned by Monsanto Company, addressing various aspects of the toxicity of glyphosate and glyphosate-based formulations, were submitted to Critical Reviews in Toxicology, subjected to rigorous external review, revised and published in CRT prior to the IARC meeting (Kimmel et al. 2013; Kier & Kirkland 2013; Kier 2015; Greim et al. 2015). Those papers were frequently accessed on-line and, most importantly, copies were provided to IARC prior to the meeting of the IARC review panel in Lyon, France in March 2015.

The IARC Panel classified glyphosate in Category 2a, probably carcinogenic to humans. At the conclusion of the review, IARC released a press announcement reporting key results of the review; this was followed by publication of a summary

paper (Guyton et al. 2015) and publication of a monograph (IARC 2015). The conclusions of the IARC Panel were a surprise to many scientists who had followed the literature on the potential health hazards of glyphosate over many decades. This was especially the case because the IARC classification of glyphosate as probably carcinogenic to humans ran counter to the conclusions of a number of previous carcinogenic hazard assessments conducted by multiple government agencies around the world.

Following the IARC carcinogenic hazard classification of glyphosate, the Monsanto Company engaged Intertek, a scientific and regulatory consulting firm, to convene an independent scientific panel to evaluate and synthesize the scientific evidence of the potential carcinogenic hazard of glyphosate. The activities and conclusions of the independent panel are reported in the five papers in this special issue. Each of the five papers was rigorously reviewed by 5-10 independent reviewers selected by the CRT Editor and anonymous to the authors. A total of 27 different reviewers participated with several of the individuals reviewing all five papers. The authors of each paper were provided the review comments on their paper and asked to make appropriate revisions. The final papers, published here, represented the work product of the authors. Each paper includes an Acknowledgements section and an extensive Declaration of Interest section.

In order to facilitate the broadest possible readership, Intertek requested that these five papers be published in a sponsored Open Access Supplement Issue in the 2016 volume of Critical Reviews in Toxicology. Negotiations for such sponsored supplements are customarily conducted between the sponsor and publisher, separate from the review process, thereby maintaining the journal's editorial independence. The Editor-in-Chief was not party to these negotiations.

It is anticipated that scientific discussions concerning the science of the potential carcinogenic hazards of glyphosate and its use will continue for some time along with related discussions of how this science informs policy decisions on the regulation of glyphosate-containing products. The contents of these five papers, the extensive listing of references in each paper and the Supplemental Material (available online for several of the papers), will contribute to and facilitate continued scientific discussions and policy decisions on this widely used chemical.

Acknowledgments

The Editor gratefully acknowledges the extensive review comments offered by the 27 external reviewers. Those comments enhanced the quality and completeness of the five papers.

Declaration of interest

Roger O. McClellan, the Editor-in-Chief of Critical Reviews in Toxicology (CRT), since 1987, currently serves as an independent advisor to private and public entities on environmental and occupational health issues. Early in his career, his research focused on the health effects of radiation and internally-deposited radionuclides as an employee of General Electric Company and the U.S. Atomic Energy Commission (AEC). Later he provided leadership for the Lovelace Inhalation Toxicology Research Institute's extensive research program on airborne radionuclides and other toxicants with primary financial support from the AEC and the U.S. Department of Energy. From 1988 to 1999, he was the President and Chief Executive Officer of the Chemical Industry Institute of Toxicology (CIIT), a not-for-profit research institute whose extensive research program, focusing on mechanisms of action of chemicals, was supported by dues payments from member companies. The Monsanto Company was a founding member of the CIIT. The CIIT did not conduct any research on glyphosate. McClellan, during his career, has served on over 100 major advisory committees for private firms, academic institutions and U.S. government and international agencies, including IARC. None of these advisory assignments has directly involved review of the health hazards of glyphosate. McClellan, in his role as Editor-in-Chief of CRT, selected the 27 individuals who reviewed the five papers published in this Special Supplement. The reviewers represented a cross-section of scientists from around the globe employed by academic, government and private entities or working as sole proprietors. The review comments they provided were considered to represent their independent professional views.

This article is part of a supplement, sponsored and supported by Intertek Scientific & Regulatory Consultancy. Funding for the sponsorship of this supplement was provided

to Intertek by the Monsanto Company, which is a primary producer of glyphosate and products containing this active ingredient.

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